PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Association between contact with a general practitioner and depressive symptoms during the COVID-19 pandemic and lockdown: a large community-based study in Hangzhou, China
AUTHORS	Yang, Fei; Lin, Wenhui; Frost, Eleanor; Min, Yan; Xu, Xiaochen; Wang, Xiaoyan; Li, Wei; Leng, Yue; Zhao, Xueyin; He, Wei; Hsing, Ann W.; Zhu, Shankuan

VERSION 1 – REVIEW

REVIEWER	Gainer, Danielle Wright State University, Psychiatry
REVIEW RETURNED	14-May-2021

GENERAL COMMENTS	There are numerous grammar and spelling errors. There are SEVERAL limitations to the study and biases that were not discussed. Selection bias needs to be considered and discussed. Furthermore, correlation does not equal causation and this needs to be discussed. There are a number of statements that imply causation and should be removed or re-written. A thorough discussion of the role of GPs in China should be included and a further background of the original study. Depression symptoms are NOT at all addressed by the WHO-5 - it is a measure of well being. Therefore, the manuscript should be re-written as assessment of wellbeing, no depression.

REVIEWER	Ho, Roger National University of Singapore, Department of Psychological Medicine
REVIEW RETURNED	27-May-2021

GENERAL COMMENTS	I have the following comments for the authors to address. I am happy to review this paper again. 1) Under the Introduction, the authors stated "COVID-19 is not only threatening on physical health but also impacting on short-term and long-term mental health 2 3" Reference 2 and 3 are commentary and not research studies. Please refer to the following landmark systematic review and research study instead: Impact of COVID-19 pandemic on mental health in the general population: A systematic review [published online ahead of print, 2020 Aug 8]. J Affect Disord. 2020;277:55-64. doi:10.1016/j.jad.2020.08.001

	Please discuss how physical and mental health are related during the pandemic: A chain mediation model on COVID-19 symptoms and mental health outcomes in Americans, Asians and Europeans. Sci Rep 11, 6481 (2021). https://doi.org/10.1038/s41598-021-85943-7 2) The authors stated "Psychological impacts during lockdown have been reported 5" Reference 5 does not focus on psychological impact, please refer to the following studies instead: The psychological impact of lockdown: Anxiety and Depression Among People Under the Nationwide Partial Lockdown in Vietnam. Front Public Health. 2020;8:589359. Published 2020 Oct 29. doi:10.3389/fpubh.2020.589359 The psychological Impact of social distancing: Impact of COVID-19 on Economic Well-Being and Quality of Life of the Vietnamese During the National Social Distancing. Front Psychol. 2020 Sep 11;11:565153. doi: 10.3389/fpsyg.2020.565153. PMID: 33041928; PMCID: PMC7518066. The psychological impact of face mask use: The Association Between Physical and Mental Health and Face Mask Use During the COVID-19 Pandemic: A Comparison of Two Countries With Different Views and Practices. Front Psychiatry. 2020;11:569981. Published 2020 Sep 9. doi:10.3389/fpsyt.2020.569981 3) Before the paragraph "In response to the outbreak of COVID-19 in China in late January, 2020", please discuss the findings of the following landmarks studies conducted in China: The first mental health study in China Immediate Psychological Responses and Associated Factors during the Initial Stage of the 2019 Coronavirus Disease (COVID-19) Epidemic among the General Population in China. Int J Environ Res Public Health. 2020;17(5):1729. Published 2020 Mar 6. doi:10.3390/ijerph17051729 The first longitudinal study in China: Longitudinal Study on the Mental Health of General Population during the COVID-19 Epidemic in China [published online ahead of print, 2020 Apr 13]. Brain Behav Immun. 2020; S0889-1591(20)30511-0. doi:10.1016/j.bbi.2020.04.028 Impact on psychiatric patients in China: Do psychiatric patients experience more psychiatric symptoms during COVID-19 pandemic and lockdown? A Case-Control Study with Service and Research Implications for Immunopsychiatry [published online ahead of print, 2020 Apr 27]. Brain Behav Immun. 2020;S0889-1591(20)30626-7. doi:10.1016/j.bbi.2020.04.069 Impact on workers in China: Is Returning to Work during the COVID-19 Pandemic Stressful? A Study on Immediate Mental Health Status and Psychoneuroimmunity Prevention Measures of Chinese Workforce [published online ahead of print, 2020 Apr 23]. Brain Behav

	Immun. 2020;S0889-1591(20)30603-6. doi:10.1016/j.bbi.2020.04.055 Impact on real COVID patients: A quantitative and qualitative study on the neuropsychiatric sequelae of acutely ill COVID-19 inpatients in isolation facilities. Transl Psychiatry. 2020 Oct 19;10(1):355. doi: 10.1038/s41398-020-01039-2. PMID: 33077738. 3) The authors need to provide more information about recruitment area "Gongshu District, Hangzhou, Zhejiang, " Is it urban or rural area? 4) Under the discussion, the authors stated "For example, establishment of appropriate mental health-care systems for health workers16," This seems to be irrelevant because this study is on the general population and not healthcare workers. Please refer to the following studies instead: Importance of health information during the pandemic: Coverage of Health Information by Different Sources in Communities: Implication for COVID-19 Epidemic Response. Int. J. Environ. Res. Public Health 2020, 17, 3577. Engagement with rural leaders: Reaching further by Village Health Collaborators: The informal health taskforce of Vietnam for COVID-19 responses. J Glob Health. 2020;10(1):010354. doi:10.7189/jogh.10.010354 Use of online cognitive behavior therapy to treat psychological symptoms during the pandemic: The most evidence-based treatment is cognitive behaviour therapy (CBT), especially Internet CBT that can prevent the spread of infection during the pandemic. Use of Cognitive Behavior Therapy (CBT) to treat psychiatric symptoms during COVID-19: Mental Health Strategies to Combat the Psychological Impact of COVID-19 Beyond Paranoia and Panic. Ann Acad Med Singapore. 2020;49(3):155-160. Cost-effectiveness of iCBT: Moodle: The cost effective solution for internet cognitive behavioral therapy (I-CBT) interventions. Technol Health Care. 2017;25(1):163-165. doi: 10.3233/THC-161261. PMID: 27689560. Internet CBT can treat psychiatric symptoms such as insomnia: Efficacy of digital cognitive behavioural therapy for insomnia: a meta-analysis of randomised controlled trials. Sleep Med. 2020 Aug 26;75:315-325. doi: 10.1016/j.sleep.2020.08.020. Epub ahead of print. PMID: 32950013. 5) The authors stated "Second, we defined depressive symptoms using the WHO-Five Well-being index." I agree with this limitation. Please refer to the following multi-country study in Asia and discuss the questionnaire they used to assess depression. It is more robust than this study:

	The impact of COVID-19 pandemic on physical and mental health of Asians: A study of seven middle-income countries in Asia. PLoS One. 2021 Feb 11;16(2):e0246824. doi: 10.1371/journal.pone.0246824. PMID: 33571297. Please add how to improve detection of depression. The latest is functional imaging: This study mainly used self-reported questionnaires to measure psychiatric symptoms and did not make clinical diagnosis. The gold standard for establishing psychiatric diagnosis involved structured clinical interview and functional neuroimaging (Husain et al 2019, Husain et al 2020, Ho et al 2020). References: Husain SF, Yu R, Tang TB, et al. Validating a functional near-infrared spectroscopy diagnostic paradigm for Major Depressive Disorder. Sci Rep. 2020;10(1):9740. Published 2020 Jun 16. doi:10.1038/s41598-020-66784-2 Husain SF, Tang TB, Yu R,et al . Cortical haemodynamic response measured by functional near infrared spectroscopy during a verbal fluency task in patients with major depression and borderline personality disorder. EBioMedicine. 2019 Dec 23;51:102586. doi: 10.1016/j.ebiom.2019.11.047. PMID: 31877417. Ho CSH, Lim LJH, Lim AQ, et al. Diagnostic and Predictive Applications of Functional Near-Infrared Spectroscopy for Major Depressive Disorder: A Systematic Review. Front Psychiatry. 2020;11:378. Published 2020 May 6. doi:10.3389/fpsyt.2020.00378 6) The authors should propose further research to study the impact of GP to enhance COVID-19 vaccine uptake. The authors can design a new study based on the following study to assess the impact of GP contact on willingness to receive vaccine. An Asia-Pacific study on healthcare worker's perception and willingness to receive COVID-19 vaccination. Int J Infect Dis. 2021 Mar 26:S1201-9712(21)00287-3. doi: 10.1016/j.ijid.2021.03.069. Epub ahead of print. PMID: 33781902; PMCID: PMC7997703.

VERSION 1 – AUTHOR RESPONSE

Comments from Reviewer #1

1. There are numerous grammar and spelling errors.

Author's response: Dear Reviewer, we have asked a native speaker and a senior researcher to do the proof reading, and we have corrected the spelling and grammar errors in the revised manuscript.

2. There are SEVERAL limitations to the study and biases that were not discussed. Selection bias needs to be considered and discussed.

Author's response: Dear Reviewer, thank you for your comment. We have added texts regarding limitations and biases that were not addressed in the previous version, such as association and

causation, selection bias and the generalization of our findings, etc. Please see the texts from line 323 to 324, line 324 to 334 in the revised manuscript.
Line 323 to 324: “First, causation could not be established owing to the cross-sectional design of this study.”
Line 324 to 334: “Second, selection bias may exist. During the COVID-19 epidemic, telephone interviewing was used, which may have introduced volunteer bias. To identify the potential influence of selection bias, we conducted a non-response analysis by comparing the general characteristics between the study population (n = 3,153) and the population excluded from the study (n = 991). The results showed that the study population had higher educational levels ($P < 0.05$) and had more NCDs ($P < 0.05$) than individuals who were excluded from the study (see Table S1). A potential explanation is that people with higher education levels and more health conditions may pay greater attention to their own health and would thus be more likely to participate in health-related research projects.”

3. Furthermore, correlation does not equal causation and this needs to be discussed. There are a number of statements that imply causation and should be removed or re-written.

Author’s response: We admit that correlation does not equal causation. We have changed a number of statements that imply causation and addressed this issue in the limitations of this study. Please see the texts in the revised manuscript in the title line, line 42 to 43, line 67 to 69, line 128 to 131, line 248 to 251, line 300 to 302, line 323 to 324.
Line 1: “Association between contact with a general practitioner and depressive symptoms during the COVID-19 pandemic and lockdown: a large community-based study in Hangzhou, China”
Line 42 to 43: “To determine the association of GP contact with depressive symptoms during the COVID-19 pandemic and lockdown in China.”
Line 67 to 69: “Contact with GPs during the COVID-19 pandemic and lockdowns may have a negative association with depressive symptoms in community-dwelling populations.”
Line 128 to 131: “Therefore, in the present study, we investigated the association between having contact with a GP by telephone (GP contact) and depressive symptoms among community residents before and during the COVID-19 lockdown period in Hangzhou, China.”
Line 248 to 251: “In the present study, GP contact was negatively associated with prevalent depressive symptoms and new depressive symptoms among residents of Gongshu District, Hangzhou, China during the COVID-19 pandemic and lockdown between February and March, 2020.”
Line 300 to 302: “In the present study, we found a significant negative association of GP contact with a risk of having depressive symptoms only among local residents with middle or high school educational attainment.”
Line 323 to 324: “First, causation could not be established owing to the cross-sectional design of this study.”

4. A thorough discussion of the role of GPs in China should be included and a further background of the original study.

Author’s response: Thank you for your comment. We have added a detailed statement with regard to the role of GPs in China in the ‘Introduction’ session: please see the texts in the line 100 to 114, line 115 to 116, line 121 to 124; and in the ‘Discussion’ session: line 261 to 267, and line 273 to 277.
Introduction session:
Line 100 to 114: “In China, mental health during the COVID-19 pandemic has attracted attention. Wang et al. found that during the initial stages of the outbreak in China, 16.5% of respondents to an online survey reported moderate to severe depressive symptoms[13]. A longitudinal study in a Chinese community-dwelling population showed that 4 weeks after the pandemic peak, depressive symptoms were similar to those at the initial stage, using the Depression, Anxiety and Stress Scale (DASS) depression subscale[14]. Additionally, some surveys have focused on depression in a specific population, such as patients with COVID-19, psychiatric patients, and workers returning to the workplace after lockdown. Results from these studies suggest that patients with COVID-19 and

psychiatric patients are more vulnerable to and have relatively high levels of depression.[15-17] Studies have shown that personal precautionary measures, confidence in doctors, and satisfaction with health education may relieve depression and anxiety. [13 14 18] Chinese general practitioners (GPs) may play an essential role during the pandemic by giving professional support to people at risk of impaired mental health."
Line 115 to 116: "Community-based prevention and control of mental diseases (or mental health) are important for controlling the COVID-19 pandemic[19]."
Line 121 to 124: "Normally, GPs are involved in health improvement and the control of noncommunicable diseases (NCDs)[21 22]. During the COVID-19 epidemic in China, GPs hve contacted residents with or without NCDs via telephone."
Discussion session:
Line 261 to 267: "GPs are the foundation of community health services, including prevention, health education, basic clinical services, women and children's care, elder care, immunization, and physical rehabilitation.[37] In China, GPs are also known as family doctors or family physicians. In 2015, these contract services were implemented throughout Zhejiang Province[38]. A previous study reported that services for mental health management had improved depressive symptoms among local residents via health education and organizational interventions [39]."
Line 273 to 277: "In the battle against COVID-19, GPs have been involved in all aspects of the pandemic response. GPs with good communication skills work with local community staff to perform daily health monitoring and provide psychological support to help relieve fear and panic, such as through psychological counseling via telephone- and internet-based communication."

5. Depression symptoms are NOT at all addressed by the WHO-5 - it is a measure of well being. Therefore, the manuscript should be re-written as assessment of wellbeing, no depression.

Author's response: Thank you for your comment. We agree with you that WHO-5 is not a direct measurement of depression. Based on the literature review, WHO-5 can be used as a sensitive and specific screening tool for depression, and has a relatively good performance in terms of clinical metrics, including reliability and validity. Thus, it can be used as an indicator of depression or depressive symptoms in clinical trial, covering a wide range of study fields [reference: Topp CW, Ostergaard SD, Sondergaard S, et al. The WHO-5 Well-Being Index: a systematic review of the literature. Psychother Psychosom 2015;84(3):167-76].
We have added several lines of texts regarding the reason why we used WHO-5 in methods session, as well as the texts regarding the potential limitation that may be caused by using WHO-5 to measure depressive symptoms. Please see line 159 to 165 and line 334 to 340 in the revised manuscript.
Methods:
Line 159 to 165: "Although the WHO-5 is not considered the gold standard for defining depression, it has relatively good psychometric performance in terms of reliability and validity, and it has a strong correlation with depressive symptoms. [26] The WHO-5 can be used as a sensitive and specific screening tool for depression in epidemiological studies. Considering the time limit of telephone interviews, we chose to use the WHO-5 as an indicator of depressive symptoms in this large population health survey."
Discussion:
Line 334 to 340: "Third, we defined depressive symptoms using the WHO-5, whose psychometric performance is not the same as that of traditional measures of depression, such as Zung's Self-Rating Depression Scale [45] and the 21-item DASS [18]. We recommend that future studies apply multiple approaches to precisely measure depression, including short-version screening tools, gold standard instruments, and clinical diagnosis, such as structured clinical interviews and functional neuroimaging[46-48]."

Comments from Reviewer #2

1. Under the Introduction, the authors stated "COVID-19 is not only threatening on physical health but also impacting on short-term and long-term mental health 23" Reference 2 and 3 are commentary and not research studies. Please refer to the following landmark systematic review and research study instead; Please discuss how physical and mental health are related during the pandemic.

Author's response: Dear Reviewer, thank you for your comment. We have replaced references 2 and 3 with the landmark systematic review and research study you recommended, and we discussed how physical and mental health are related during the pandemic by adding texts from line 83 to 88 in the revised manuscript.

Line 83 to 88: "According to reports, the rate of depressive symptoms in the general population was 14.6%–48.3% during the COVID-19 epidemics in China, Spain, Italy, Iran, the United States, Turkey, Nepal, and Denmark, using different measurement tools[2]. Furthermore, physical symptoms similar to COVID-19 infection can increase people's perceived risk and lead to adverse mental health outcomes, including depressive symptoms[3]."

2. The authors stated "Psychological impacts during lockdown have been reported 5" Reference 5 does not focus on psychological impact, please refer to the following studies instead:

Author's response: Thank you for your comment. We have carefully read the studies you listed and cited it instead of Reference 5. Please see line 93 to 97 in the revised manuscript.

Line 93 to 97: "Psychological impacts during lockdowns have been reported[5-8]. Stressful life events, pessimism, home quarantine, social distancing, wearing face masks, and increased exposure to social media have been reported to influence mental health during lockdown, exacerbating various mental health conditions, including depression, anxiety, and grief-related symptoms[9-12]."

3. Before the paragraph "In response to the outbreak of COVID-19 in China in late January, 2020", please discuss the findings of the following landmarks studies conducted in China; The authors need to provide more information about recruitment area "Gongshu District, Hangzhou, Zhejiang, " Is it urban or rural area?

Author's response: Thank you for your comment. We have carefully read the landmarks studies conducted in China and discussed before the paragraph "In response to the outbreak of COVID-19 in China in late January, 2020"; and we have further explained the regional attribute of the recruitment area "Gongshu District, Hangzhou, Zhejiang, ". Please see line 100 to 114 and line 135 to 138 in the revised manuscript.

Line 100 to 114: "In China, mental health during the COVID-19 pandemic has attracted attention. Wang et al. found that during the initial stages of the outbreak in China, 16.5% of respondents to an online survey reported moderate to severe depressive symptoms[13]. A longitudinal study in a Chinese community-dwelling population showed that 4 weeks after the pandemic peak, depressive symptoms were similar to those at the initial stage, using the Depression, Anxiety and Stress Scale (DASS) depression subscale[14]. Additionally, some surveys have focused on depression in a specific population, such as patients with COVID-19, psychiatric patients, and workers returning to the workplace after lockdown. Results from these studies suggest that patients with COVID-19 and psychiatric patients are more vulnerable to and have relatively high levels of depression.[15-17] Studies have shown that personal precautionary measures, confidence in doctors, and satisfaction with health education may relieve depression and anxiety. [13 14 18] Chinese general practitioners (GPs) may play an essential role during the pandemic by giving professional support to people at risk of impaired mental health."

Line 135 to 138: "Telephone interviews were conducted in April 2020 among 4,144 urban residents who participated in the baseline survey of the Stanford Wellness Living Laboratory-China (WELL China) study between October 2018 and May 2019 in Gongshu District, Hangzhou City in Zhejiang, China, which is an urban area.[25]."

4. Under the discussion, the authors stated "For example, establishment of appropriate mental health-care systems for health workers16," This seems to be irrelevant because this study is on the general population and not healthcare workers. Please refer to the following studies instead.

Author's response: Thank you for your comment. We have revised the discussion accordingly. In the revised texts, we addressed that current mental health management strategies also are applied to the general population, and we added some strategies such as Cognitive Behavior Therapy (CBT) and the dissemination and utilization of health information. Please see line 253 to 260 in the revised manuscript.

Line 253 to 260: "Some strategies have been proposed for managing mental health during the pandemic. Although patients with or survivors of COVID-19[28], patients with severe mental illness[29], and health care workers[30] require mental health care, the general public also requires mental health attention during the COVID-19 pandemic and lockdown periods. Online-based cognitive behavioral therapy may be one effective solution[31-33]. It is also important to promote communication of up-to-date information on the prevention and control of COVID-19 in consideration of mental health content[34 35]. Improving management of community-based primary mental health care is an important goal[36]."

5. The authors stated "Second, we defined depressive symptoms using the WHO-Five Well-being index." I agree with this limitation. Please refer to the following multi-country study in Asia and discuss the questionnaire they used to assess depression. It is more robust than this study; Please add how to improve detection of depression. The latest is functional imaging.

Author's response: Thank you for your comment. We have referenced the multi-country study in Asia and discussed the questionnaire they used to assess depression; we also have added the latest methods to improve the screening of depression. Please see line 334 to 340 in the revised manuscript.

Line 334 to 340: "Third, we defined depressive symptoms using the WHO-5, whose psychometric performance is not the same as that of traditional measures of depression, such as Zung's Self-Rating Depression Scale [45] and the 21-item DASS [18]. We recommend that future studies apply multiple approaches to precisely measure depression, including short-version screening tools, gold standard instruments, and clinical diagnosis, such as structured clinical interviews and functional neuroimaging[46-48]."

6. The authors should propose further research to study the impact of GP to enhance COVID-19 vaccine uptake. The authors can design a new study based on the following study to assess the impact of GP contact on willingness to receive vaccine.

Author's response: Thank you for your comment. We have pointed out the need for further research to study the impact of GP to enhance COVID-19 vaccine uptake. Please see line 352 to 354 in the revised manuscript.

This is an interesting and meaningful idea. If we have the opportunity, we will conduct a new research design to assess the impact of GP contact on willingness to receive vaccine.

Line 352 to 354: "Additionally, with the advancement of COVID-19 vaccine development together with the existing problem of vaccine hesitancy[52], it is necessary to explore the impact of GPs on COVID-19 vaccine uptake in future studies."

VERSION 2 – REVIEW

REVIEWER	Ho, Roger National University of Singapore, Department of Psychological Medicine
REVIEW RETURNED	29-Jul-2021

GENERAL COMMENTS	I recommend publication.